Summary of Investigation Results

Sodium valproate

August 27, 2024

Non-proprietary name

Sodium valproate

Brand name (marketing authorization holder)

Depakene Tablets 100 mg, 200 mg, Depakene R Tablets 100 mg, 200 mg, Depakene Fine Granules 20%, 40%, Depakene Syrup 5% (Kyowa Kirin Co., Ltd.), Selenica-R Granules 40%, Selenica-R Tablets 200 mg, 400 mg (Kowa Company, Ltd.), and the others

Japanese market launch

Depakene Tablets 100 mg: September 1981

Depakene Tablets 200 mg, Depakene Syrup 5%: March 1975

Depakene R Tablets 100 mg, 200 mg: January 1991

Depakene Fine Granules 20%: October 1987

Depakene Fine Granules 40%: June 1984

Selenica-R Granules 40%: December 1991

Selenica-R Tablets 200 mg: July 2004

Selenica-R Tablets 400 mg: July 2006

Indications

・Treatment of various types of epilepsy (petit mal, focal seizure, psychomotor seizures, and mixed seizure) and personality or behaviour disorder (bad mood, irritability, etc.) associated with epilepsy

・Treatment of mania, manic state in manic depressive illness

・Prevention of migraine attacks

Summary of revisions

Information on the occurrence of neurodevelopmental disorder in infants/children with paternal exposure to sodium valproate should be added to the 15.1 Information Based on Clinical Use section in 15. OTHER PRECAUTIONS.

Investigation results and background of the revision

Published articles on overseas epidemiological studies regarding neurodevelopmental disorder in infants/children with paternal exposure to sodium valproate were evaluated. As a result of consultation with expert advisors, although evaluation of the risk of neurodevelopmental disorder in infants/children with paternal exposure to sodium valproate has not been established, the MHLW/PMDA concluded that revision of PRECAUTIONS was necessary, since the possibility of occurrence of neurodevelopmental disorder in infants/children with paternal exposure to sodium valproate cannot be ruled out, taking into consideration the following:

- An observational study performed in Scandinavian countries* suggested that infants/children with paternal exposure to sodium valproate within 3 months prior to conception had an increased risk of developing neurodevelopmental disorder. Of note, performing a new study for further investigation has been required in Europe†.
- An overseas observational study in fathers with epilepsy (JAMA Netw Open. 2024; 7: e2414709) showed that infants/children with paternal exposure to sodium valproate within 120 days prior to conception did not have a statistically significant increased risk of neurodevelopmental disorder.

* PASS -Paternal exposure to valproate -Updated Abstract Following Reanalysis of Norway Data of Corrigendum to Final Study Report Version 1.1 and Addendum Version 2 Valproate EU consortium Stand Alone Abstract V2.0
(https://catalogues.ema.europa.eu/system/files/2024-02/Valproate_PASS_Abstract_V2.0_0.pdf)

† Assessment report by the Pharmacovigilance Risk Assessment Committee of the European Medicines Agency (EMA)
(https://www.ema.europa.eu/en/documents/other/valproate-prac-non-interventional-imposed-pass-final-study-report-assessment-report-emea-h-n-psr-j-0043_en.pdf)

The expert advisors present at the Expert Discussion regarding the current investigation were nominated based on their

conflict of interest declarations concerning the relevant products, pursuant to the “Rules for Convening Expert Discussions, etc., by the Pharmaceuticals and Medical Devices Agency” (PMDA Administrative Rule No. 20-8, dated December 25, 2008).